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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,331	09/11/2006	Shawn DeFrees	040853-01-5128US	2246

43850 7590 01/21/2009

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
01/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,331	DEFREES ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-25* is/are pending in the application.

4a) Of the above claim(s) *14-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1 and 3-25 are pending.

2. Claims 14-25 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a non-elected invention.

3. Claims 1 and 3-13, drawn to a compound having the formula: Ab-G-L-T, are being acted upon in this Office Action.

4. In view of the claims amendment filed October 30, 2008, the following objection and rejections remain.

5. The specification stands objected to as failing to provide proper antecedent basis for the claimed subject matter of claim 11. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification fails to provide proper antecedent basis for the formula recited in original claim 11. Amendment to the specification to include the formula as recited in claim 11 is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 and 3-13 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

According to MPEP 2163, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba,*

B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co. the court stated: "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it

is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In Gostelli, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) level of skill and knowledge in the art, (2) partial structure, (3) physical and/or chemical properties, (4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) method of making the claimed invention.

In the instant case, Claim 1 encompasses a genus of compound having the formula: Ab-G-L-T wherein Ab is any antibody, G is any intact glycosyl linking group, L is any bond or any spacer moiety covalently joining G to T and T is any toxin.

Claims 4-6 encompass any compound having the structure as set forth in claim 4 wherein L1 is any bond or any linker moiety, A is any amplifier moiety, or any dendrimer.

At the time of filing, the specification discloses only the specific monoclonal antibodies that bind to CD20, CD3, TNF receptor, CD4, CEA, EGF or HER-2 receptor covalently linked to toxin via O-glycosylation through a pacer such as polyethylene glycol, polylysine, or dendrimer PAMAM, sugar, see pages 19 and 38.

The specification does not describe other conjugates comprising any members of the antibody glycosylated linked to any toxin. The specification does not describe the binding specificity associated with the complete structure of any antibody for the claimed compound. The specification does not adequately describe the common structural attribute, i.e., intact glycosyl linking group other than the O-linked glycosylation site for an attachment of one sugar selected from the group consisting of acetylgalactosamine, galactose, manose, GlcNAc, glucose, fucose or xylose.

The state of the art at the time of filing is such that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable

regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRS (all six CDRs) in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979-1983, 1982; PTO 892). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding.

Barrios et al (J Molecular Recognition 17: 332-338, 2004; PTO 892) teach the amino acid residues in the CDRs and the length of the antibody heavy chain complementarity determining region (CDR3) are critical for antigen specific binding site (see abstract, in particular). The length of the amino acid sequence that linked the CDRs of immunoglobulin light and heavy chains is important in maintaining their required conformation for binding and in vivo activity.

Further, the function of an antibody molecule is dependent on its three dimensional structure, which in turn is dependent on its primary amino acid sequence. Changing the amino acid sequence of an antibody may adversely affect its activity. Likewise, fragments of the antibody may not retain the appropriate three-dimensional structures necessary to foster binding activity. There are also critical framework residues which are also important in positioning the CDRs for interaction with antigen or which are involved in interactions between the heavy and light chains. There is no guidance as to which residues in all antibodies and toxins the attachment site and whether the antibody retains antigen binding and the toxin activity remain uncompromised.

Further, there is no single species of antibody-toxin conjugate has been disclosed to have targeting toxin to the site of interest. There is insufficient description of a common core structure that would allow one of skill in the art to practice the invention as claimed. The description requirement of the patent statue requires a description of an invention, not an

indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of antibody covalently linked to a genus of intact glycosyl linking group or to a genus of spacer moiety to a genus of toxin as claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115). Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1103, Friday April 11, 2004.

Applicants' arguments filed October 30, 2008 have been fully considered but are not found persuasive.

Applicants' position is that instant specification explicitly disclosed antibodies that can bind to, e.g. CD20, CD3, TNF receptor, CD4, CEA, EGF and HER-2 receptor. Given that "antibody" is an art-recognized term, the present disclosure, inter alia pg. 19 and 38, is sufficient to inform those skilled in the art that the applicant was in possession of the claimed composition, without having to recite ad nauseum every antibody known in the art.

In response, the claims are NOT drawn to the specific antibodies disclosed in the specification as argued. The claims are drawn to any compound or conjugate comprising any antibody, linked to any toxin via any intact glycosyl linking group such as any bond or any spacer moiety, any amplifier moiety, any amplifier moiety such as polyamine, polyethylene glycol.

At the time of filing, the specification discloses only the specific monoclonal antibodies that bind to CD20, CD3, TNF receptor, CD4, CEA, EGF or HER-2 receptor covalently linked to toxin via O-glycosylation through a pacer such as polyethylene glycol, polylysine, or dendrimer PAMAM, sugar, see pages 19 and 38.

The specification does not describe other conjugates comprising any members of the antibody glycosylated linked to any toxin. The specification does not describe the binding specificity associated with the complete structure of any antibody for the claimed compound. The specification does not adequately describe the common structural attribute, i.e., intact glycosyl linking group other than the O-linked glycoxylation site for an attachment of one sugar selected from the group consisting of acetylgalactosamine, galactose, manose, GlcNAc, glucose, fucose or xylose.

The state of the art at the time of filing is such that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRS (all six CDRs) in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979-1983, 1982; PTO 892). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding.

Barrios et al (J Molecular Recognition 17: 332-338, 2004; PTO 892) teach the amino acid residues in the CDRs and the length of the antibody heavy chain complementarity determining region (CDR3) are critical for antigen specific binding site (see abstract, in particular). The length of the amino acid sequence that linked the CDRs of immunoglobulin light and heavy chains is important in maintaining their required conformation for binding and in vivo activity.

Further, the function of an antibody molecule is dependent on its three dimensional structure, which in turn is dependent on its primary amino acid sequence. Changing the amino acid sequence of an antibody may adversely affect its activity. Likewise, fragments of the antibody may not retain the appropriate three-dimensional structures necessary to foster binding

activity. There are also critical framework residues which are also important in positioning the CDRs for interaction with antigen or which are involved in interactions between the heavy and light chains. There is no guidance as to which residues in all antibodies and toxins the attachment site and whether the antibody retains antigen binding and the toxin activity remain uncompromised.

Further, there is no single species of antibody-toxin conjugate has been disclosed to have targeting toxin to the site of interest. There is insufficient description of a common core structure that would allow one of skill in the art to practice the invention as claimed. The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of antibody covalently linked to a genus of intact glycosyl linking group or to a genus of spacer moiety to a genus of toxin as claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Leung et al (of record, J Immunology 154: 5919-5926, 1995; PTO 1449).

Leung et al (J Immunology 154: 5919-5926, 1995; PTO 1449) teaches a compound such as Ab -G-L-T wherein Ab is an antibody, G is an intact glycosyl linking group covalently joining Ab to L; L is a bond and T is a cytotoxic agent doxorubicin or toxin (see page 5922, Figure 2, schematic representation of antibody hMN-14N or fragment thereof Fab2 having glycosyl linking group Asn-X-Ser/Thr covalently linked to H2N represent by chelator/drugs/toxin, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed October 30, 2008 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended by incorporating the limitations of claim 2 into claim 1.

In response, it is noted that amended claim 1 recites a compound having the formula: Ab-G-L-T wherein

Ab is an antibody;
G is an intact glycosyl linking group covalentlyjoining Ab to L;
L is a bond **or** a spacer moiety covalently joining G to T; and
T is a toxin, wherein
said spacer moiety is a member selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl moieties.

The claimed compound encompasses antibody linked to toxin via a glycosyl bond **or** the antibody linked to a toxin via a spacer moiety is a member selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl moieties.

Leung et al (J Immunology 154: 5919-5926, 1995; PTO 1449) teaches a compound such as Ab -G-L-T wherein Ab is an antibody, G is an intact glycosyl linking group covalently joining Ab to L; L is a bond and T is a cytotoxic agent doxorubicin or toxin (see page 5922, Figure 2, schematic representation of antibody hMN-14N or fragment thereof Fab2 having glycosyl linking group Asn-X-Ser/Thr covalently linked to H2N represent by chelator/drugs/toxin, in particular). Thus, the reference teachings anticipate the claimed invention.

10. Claims 1 and 3-9 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No 7,125,843 (of record, filed April 9, 2003 claimed earliest priority to Oct 10, 2001; PTO 892).

The '843 patent teaches a compound such as a conjugate comprising a peptide or an antibody targeting moiety such as anti-CD20 antibody (see col. 67, line 48-67, col. 143, line 34-41, col. 141, line 30-42, col. 339, line 1-13, in particular), an intact glycosyl linking group via a O-linked glycans originating from serine or threonine (see col. 12, line 33-35, col. 67, line 55-56, in particular) interposed between the antibody and the selected therapeutic moiety such as a toxin or cytotoxic agents, e.g. adriamycin, doxorubicin and taxol (see entire document col. 145, lines 66 through col. 146, line 5, col. 67, line 34-67, col. 67, line 18, col. 68, line 63, Table 2, col. 84, line 46-67, col. 166, line in particular). The reference linking moiety can be either a bond or a polyethylene glycol moiety or amplifier moiety (see col. 68, line 13-15, in particular). The reference PEG linker moiety can be linear or branched such as PEG comprises alkyl group (see col. 69, line 34-60, col. 75, line 66, col. 77, lines 7-8, in particular). The reference linker moiety can be alkyl, benzyl or aryl (see col. 77, line 23-32, in particular). The reference conjugate further comprises an amplifier moiety such as multiple PEG, polypropylene glycol (PPG) or alkylated amine (see col. 77, line 45-50, col. 147, line 46-52, in particular) or polyamine such as polylysine, polyaspartic acid, polyglutamate (see col. 75, line 20-21, col. 79, line 60-67, col. 166, lines 15-21, in particular). Those of skill in the art will appreciate that the conjugates between more than two peptides by, for example, by the use of a branched PEG, dendrimer, poly(amino acid), polysaccharide or the like (see col. 69, paragraphs 457-459, in particular). The PEG linker that includes two glycosyl groups is for purposes of clarity and should not be interpreted as limiting the identity of linker arms of use in this embodiment of the invention. Thus, a PEG moiety is functionalized at a first terminus with a first glycosyl unit and at a second terminus with a second glycosyl unit. The first and second glycosyl units are preferably substrates for different transferases, allowing orthogonal attachment of the first and second peptides or antibodies to the first and second glycosyl units, respectively. In practice, the (glycosyl).sup.1-PEG-(glycosyl).sup.2 linker is contacted with the first peptide and a first transferase for which the first glycosyl unit is a substrate, thereby forming (peptide).sup.1-(glycosyl).sup.1-PEG-(glycosyl).sup.2. The first transferase and/or unreacted peptide or antibody is then optionally removed from the reaction mixture. The second peptide or antibody and a second transferase for which the second glycosyl unit is a substrate are added to the (peptide).sup.1-(glycosyl).sup.1-PEG-(glycosyl).sup.2 conjugate, forming (peptide).sup.1-(glycosyl).sup.1-PEG-(glycosyl).sup.2-

(peptide).sup.2. Claim 10 is included in this rejection because the reference antibody is lined to a sugar via O-link to polymer such as polyethylene glycol that includes one or more (CH2)m from 0 to 20 and Z is a bond or OCH2CH2 (see col.75, lines 55 through col. 77, lines 61, in particular) and a cleavable linker groups (see col. 173, lines 4-25, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed October 30, 2008 have been fully considered but are not found persuasive.

Applicants' position is that Patent No. '843 teaches conjugates having the following general structure as shown at page 15 of the amendment.

In which the symbols a,b,c,d and s represent a positive non-zero integer and t is either 0 or positive integer. The "agent" is therapeutic agent, a bioactive agent, a detectable label, water-soluble moiety, or the like. The "agent" can be a peptide, e.g., enzyme, antibody, antigen, etc. The linker can be any of a wide array of linking groups. Alternatively, the linker may be a single bond or a "zero order" linker. The identity of the peptide is without limitation.

This is readily distinguishable from our compounds, which are characterized by the formula Ab-G-L-T.

In response, in addition to what applicants describe as the teachings of the '843 patent, the '843 patent further teaches a compound such as a conjugate comprising an antibody targeting moiety such as anti-CD20 antibody (see col. 67, line 48-67, col. 143, line 34-41, col. 141, line 30-42, col. 339, line 1-13, in particular), an intact glycosyl linking group or glycosylated linking bond such as a O-linked glycans originating from serine or threonine (see col. 12, line 33-35, col. 67, line 55-56, in particular) interposed between the antibody and the selected therapeutic moiety such as a toxin (see entire document col. 145, lines 66 through col. 146, line 5, col. 67, line 34-67, col. 67, line 18, col. 68, line 63, Table 2, col. 84, line 46-67, col. 166, line in particular).

Further, amended claim 1 recites a compound having the formula:
Ab-G-L-T wherein

Ab is an antibody;
G is an intact glycosyl linking group covalentlyjoining Ab to L;
L is a bond **or** a spacer moiety covalently joining G to T; and
T is a toxin, wherein

said spacer moiety is a member selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl moieties.

The claimed compound encompasses antibody linked to toxin via a glycosyl bond **or** the antibody linked to a toxin via a spacer moiety is a member selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl moieties.

Although claim 1 has been amended, the term "or" at line 6 wherein L encompasses any bond *or* a spacer moiety. The '843 patent teaches the linking group is an O-linked glycan bond (see col. 12, line 33-35, col. 67, line 55-56, in particular). Finally, the reference linking moiety can be a polyethylene glycol moiety or amplifier moiety (see col. 68, line 13-15, in particular).

11. Claims 1, 3-4, 7 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No 6,743,896 (of record, filed Sept 20, 2001 claimed earliest priority to June 23, 1997; PTO 892).

The '896 patent teaches a compound comprising a single chain antibody such as SCA, an intact glycosyl linking group such as N-linked glycosylated covalently attached to a toxin via a bond (see col. 29, line 32-33, col. 30, line 39-60, col. 29, line 20-23, claims 1, 10-11 of the '896 patent, in particular). The reference liker moiety is a member of the alkyl group (see coll. 27, line 30-36, in particular). The spacer moiety may be a heteroalkyl, alkoxyl, alky moieties (see col. 28, line 15-20, in particular). The '896 patent further polyethylene glycol or activated polyalkylene oxide (PAO) as a linker moiety attached to the carbohydrate (see col. 28, line 65-col. 42, line 39-40, in particular). The reference polyethylene glycol (PEG) can be straight chain (see col. 22, line 25-58, in particular) or branched (see col. 28, line 24-45, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed October 30, 2008 have been fully considered but are not found persuasive.

Applicants' position is that the instant application is entitled to a priority date of September 2, 2003 while U.S. Patent No. 6,743,896 was issued on June 1, 2004.

In response, the examiner apology for the inadvertent typographical error. Reading the second line of the rejection "(*filed Sept 20, 2001* claimed earliest priority to June 23, 1997; PTO 892)" is clear that it was meant to be rejected under 35 U.S.C. 102(e) instead of 102(b).

12. The following new grounds of rejections are necessitated by the amendment filed October 30, 2008.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

14. Claims 4 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 10, 11 and 12 are indefinite because the metes and bounds of what would constitute an "amplifier moiety" cannot be determined since the term "amplifier moiety" is not defined in the specification nor in said claims.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No 5,635,603 (newly cited, issued June 3, 1997; PTO 892).

The '603 patent teaches glycosylation site specific conjugation of toxin to antibody by introducing Asn glycosylation site to the antibody. The '603 patent teaches a compound such as an immunoconjugate having the following formula such as single chain antibody or antibody, a glycosylated linking group such as N-linked glycosylation sequence (also known as Asn-linked glycosylaltion site for carbohydrate such as oligosaccharide addition) as the G moiety covalently joining the antibody to a toxin such as ricin (see col. 14, line 54-55, in particular) via the side chain amino group of Asn known to one skilled in the art (see col. 9, lines 21 through col. 10, line 36, in particular) and an amplifier moiety such as polyamine, diamine, polyethylene, polyamidoamine dendrimer (see col. 14, line 20-35, col. 15, line 21-40, in particular). The '603 patent further teaches the carbohydrate (sugar) moiety on the antibody can also be attached to at least one polyethyleneglycol (PEG) (see col. 16, line 37-67, col. 17, in particular). The reference dentrimer can be linear with known number of polyamine groups or branched such as bearing

tertiary amine groups such as lysine residues, glutamate or aspartate residues attached to the toxin (see col. 15, line 21-30, in particular). The oxidized carbohydrate on the antibody can react with the aldehyde, ketone or carbonyls (see col. 15, line 47-51, in particular) or alky, acyl or combination thereof (see col. 21, lines 7-10, in particular). Thus, the reference teachings anticipate the claimed invention.

17. Amended claims 10-13 stand unsearchable because the term “L” is not defined in any of the formulas recited in claims 10-13 and the term "A, the amplifier moiety" is not defined in said claims.

18. No claim is allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O’Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

21. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
January 16, 2009